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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> Hormone Replacement Therapy (HRT) has been shown to increase breast cancer risk as well as to increase breast density. Breast density, a reflection of the histologic composition of the breast, is one factor shown to affect mammographic sensitivity and specificity, and it is predictive of breast cancer risk. Thus, the use of HRT, through its effect on breast density, may compromise the well-established reduction in mortality gained by mammographic screening. However, not all women on HRT will experience an increase in breast density. We propose a novel hypothesis to explain in part the individual variability in breast density seen among women on HRT: <i>differences in breast density are associated with differences in estrogen metabolism, and this association may be attenuated by individual factors such as body mass index and HRT regimen.</i> Our work and the work of others provide compelling evidence to support this hypothesis. To date 212 cases and 399 healthy women have been enrolled in this study.					
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## **Introduction**

The specific objective of this proposal is to begin to understand factors associated with individual variability in breast density including HRT, BMI and estrogen metabolism. Our rationale is that by understanding factors that affect breast density, we can improve breast cancer screening as well as to identify women at an increased risk of breast cancer. We will accomplish this objective by pursuing the following specific aim: to determine the effects of serum markers of estrogen metabolism, body mass index (BMI), and hormone replacement therapy (HRT) on postmenopausal breast density. This is an observational study within an ongoing study of the relationship between HRT, estrogen metabolism and breast cancer (PA State 2777693, Modugno, PI). We will measure estrogen metabolite levels and mammographic density in a group of 300 postmenopausal women (150 HRT users, 150 non-users), and correlate metabolite levels with qualitative and quantitative measures of breast density.

## **Body**

### **Work Plan: Research Proposal**

We have completed enrollment with a total of 399 controls from the Magee-Womens Hospital system. Recruiting women currently on hormone replacement therapy (HRT) remained an issue after the Women's Health Initiative (WHI) publications revealed risks of HRT use. Despite our efforts, the number of women presenting on HRT was substantially less than what was observed during the first year of recruitment. The final dataset consists of approximately 25% of the controls on HRT at enrollment (N=99). For all women recruited, blood has been processed and stored, mammographic films have been collected and a take home questionnaire was given to each subject. All data forms for women recruited to the study have been entered. Upon receipt of the questionnaire, it was reviewed for any discrepancies or blanks. If needed, the subject was called for clarification. All data has been entered into the database and after the first key entry, a set of edit checks were run to identify data entry errors as well as inconsistent responses. The edit checks were then addressed and a second key entry was performed. Finally, the two data sets were compared and reconciled. To date all subjects' data has been entered and cleaned. The mean age is 54.99, 93.5% are Caucasian, and the average body mass index (BMI) is 74.39.

All serum samples were sent to Immuna Care for estrogen metabolism testing with blinded duplicates to check for reproducibility. All samples were given random numbers and were placed in a randomly generated order in boxes to ensure that the processing of the samples was blinded. The mean levels of 2OH, 16 $\alpha$ -OH, and 2OH/16 $\alpha$ -OH are 272.57 pg/mL, 426.91 pg/mL, and 0.63 pg/mL respectively. All mammographic films have been sent to Martine Salane for evaluation. Of the films that have been read utilizing Wolfe's method, 4.2% are N1, 21.6% are P1, 71.2% are P2, and 2.08% are DY.

### **Work Plan: Training Proposal**

Receipt of the estrogen metabolite results was delayed until late spring/early summer due to increased projects at the lab. Full data analysis is now underway with final results and

manuscripts anticipated by 12/05. As outlined, I have attended the weekly Cancer Prevention Journal Club to discuss topics in cancer prevention, gain experience in presenting research results, and practice presentations for national meetings as well as for preparation for my defense presentation. I have also attended the annual UPCI retreat to learn about ongoing research within the university environment and those clinical grand rounds that focus on breast cancer. At present, I am in the process of preparing my dissertation documents.

**Key Research Accomplishments**

- 100% of planned recruitment completed from the Magee-Womens Hospital System
- All serum samples have been sent for estrogen metabolism analysis, results have been obtained.
- All mammographic films have been evaluated.
- All data forms double key entered and reconciled
- Final analysis underway

**Reportable Outcomes**

None to date

**Conclusions**

N/A – data analysis in progress

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